

Application No. 08/807,506
RESPONSE dated April 23, 2008
Reply to Office Action of January 23, 2008

REMARKS

After entry of the present amendment, claims 94 to 111, 133, and 136 to 141 are pending. Claims 94-103, 106, 107, 109, 110, 111, and 137-141 are rejected under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative under 35 U.S.C. § 103(a) as being obvious over, Smit et al. (Biochemical and Biophysical Research Communications, 1992, Vol. 187) (hereinafter "Smit-B"). Claims 94-100, 104-109, 133, 136, 137, 138, 140, and 141 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Smit et al. (Electrophoresis, 1994, Vol. 15, pp. 251-254) (hereinafter "Smit-E") in view of Smit-B and US 4,511,502 ("Builder"). Applicants respectfully request reconsideration and allowance in view of the remarks herein.

In both rejections, the Office Action suggests:

"It would have been obvious that the loss of IL-3 capability to bind zinc would result in an antagonistic activity of IL-3 because Smit discloses that zinc binding activity of IL-3 is involved in phosphorylation of IL-3 receptor. Thus an unmodified IL-3 ligand that is an agonist (receptor stimulator) when modified would be expected to become an IL-3 receptor antagonist (blocking receptor function and cascade of cellular events following receptor activation) as a results of the loss of its agonist activity due to inability to bind zinc. Thus the skilled artisan would have expected that loss of zinc binding activity of IL-3 will result in acquired antagonistic activity as presently claimed."

(Office Action, January 23, 2008, pp. 4-5.)

Applicant respectfully disagrees that the cited art supports such a conclusion. As understood by one of ordinary skill, for antagonistic activity, the inactive molecule must still be able to bind to the receptor. Antagonistic activity generally is the result of modification with the right reagent under the right conditions. In this case, the cited art provides no reasonable expectation of success that modification of a cytokine would lead to antagonistic activity in which the IL-3 still has the ability to bind to the target receptor. To the contrary, it is much more likely that modification of the zinc binding ability of IL-3 would lead to the

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mere inactivation of the molecule (*i.e.*, the molecule will have a diminished function or does not perform any function at all).

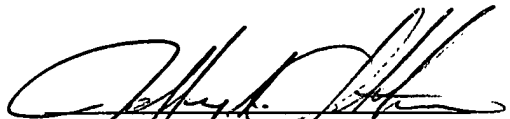
Cited concurrently with this response is an Information Disclosure Statement citing Cunningham et al. "Zinc Mediation of the Binding of Human Growth Hormone to the Human Prolactin Receptor," *Science*, Vol. 250, pages 1709-1712 (1990) (hereinafter "Cunningham"). Cunningham describes that binding human growth hormone (hGH) to a receptor was increased by about 8000-fold by the addition of 50 micromolar $ZnCl_2$. (Cunningham, p. 1709.) The growth hormone and receptor were indicated as being homologous to cytokines and IL-3. (*Id.* at 1712.) Cunningham further suggests that by modifying the zinc binding ability of hGH it will reduce the hormone's affinity for the receptor. (*see Id.* at 1710.)

Accordingly, based on the art of record, it is expected that the modification of the zinc binding ability of IL-3 would also harm its ability to bind to the target receptor. As a result, such modified molecule would not result in an antagonistic activity as urged by the Office Action because, as stated above, antagonistic activity requires the molecule to retain its ability to bind to the receptor.

Applicants respectfully request entry of the present amendment, reconsideration, and withdrawal of the rejections to claims 94 to 111, 133, and 136 to 141, and this application passed to allowance. The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,
FITCH, EVEN, TABIN & FLANNERY

Dated: April 23, 2008


Jeffrey A. Chelstrom
Registration No. 57,915

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120 South LaSalle Street, Suite 1600
Chicago, Illinois 60603-3406
Telephone (312) 577-7000
Facsimile (312) 577-7007
507644